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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/527,767	03/17/2000	Wolfgang Kreiss	LeA 33 072	3608

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EXAMINER
YANG, NELSON C

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/527,767	KREISS ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's argument regarding the previous Non-Responsive Amendment, filed March 26, 2003, with respect to the non-responsive amendment has been fully considered and is persuasive. The previous amendment has been entered and is under examination.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, claim 28 claims as part of the sensor system a support for the substance to be detected, but no mention of the support is found in the specification. The specification does teach a carrier which a sample is initially put onto or into the surface of. If applicant is referring to the carrier, the claim should be changed to refer to "a carrier" instead of "a support".

4. Claims 38-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In claim 38, applicant claims a diffusion-controlling matrix that contains "about 2 to 8 ml" of reporter gene suspension per 50 ml of matrix composition, which could presumably include less than 2 ml or more than 8 ml of reporter gene suspension per 50 ml of matrix composition. In the specification, however, applicant teaches a diffusion-controlling matrix that contains 2 to 8 ml, particularly preferably 3-5 ml, of reporter gene cell suspension, in 50 ml of sensor layer composition. Thus it would be possible for the claims to include subject matter not found within the specification, such as 1ml or 9 ml of reporter gene suspension per 50 ml of matrix composition. This is also the case where applicant claims "about 3 to about 5ml" of reporter gene suspension in claim 39, a biological sensor with an optical density of "about 0.6 to about 1.4 at 660 nm" in claim 40, a diffusion-controlling matrix with a thickness of "about 0.1 to about 10.0 mm", "about 0.5 to about 3 mm" and of "about 0.5 to about 0.8 mm" in claims 41-43.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 27-29, 31, 32, 34, 35, 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Sachs et al [US 5,942,409].

Sachs et al disclose a cytosensor microphysiometer for screening and identifying biological effects or activity/inhibition of substances (see column 7, lines 45-59 and column 8). The substances are directed against urel-dependent mechanisms maintaining bacterial metabolism and viability in acidic media (see column 4, lines 12-65). Specifically, Sachs et al disclose a cytosensor layer consisting of agarose and H. pylori cells suspended therein. The cells are in aqueous diffusive contact with a light addressable potentiometric pH sensor which assists in the detection process. In the presence of urea, the cytosensor is able to detect a net alkalinization of the medium during the pump off periods when the urease-positive H.pylori are retained in the pH-sensitive microphysiometer chambers. The sensor layer is perfused with buffers (balanced salt solutions), HCl and supplemented with0 glucose and glutamine to regulate the vitality of the sensor cells, and thus influencing the detection sensitivity, selectivity of the matrix (see column 15, lines 16 to column 16). The primary sensor output is in voltage and changes in unit per time are calculated by a computer (see column 14, lines 43-63).

7. Claims 27-36, 41, 42 and 44 are rejected under 35 U.S.C. 102(e) as being anticipated by Suzuki et al [US 4,939,098].

Susuki et al disclose a sensor device for the analysis of a sample fluid. The sensor device comprises a diffusion-controlling matrix composed of agarose or a synthetic polymer immobilizing reagents comprising antibodies, antigen, erythrocytes or liposomes, capable of producing multiple signals (immunoreaction, fluorescence, color changes, outflow from

capsules) in response to the presence of a substance (a component of a blood sample) (column 2, lines 35-65, column 4, lines 50-68 and column 5) which can be measured optically via fluorescence or radiation and electrically (column 4, lines 50-52). The thickness of the diffusion-controlling matrix taught by Susuki is selected depending on purpose of use, but is typically 1-2 mm (column 3, lines 25-33). The sensor device is also comprised of a glass support (column 2, lines 66-68 and column 3, lines 31-33) and a carrier in contact with the diffusion-controlling matrix in which a sample is to be developed (column 5, lines 13-18). Phosphate buffer are used as electrophoresis buffer, thus influencing the kinetics of the diffusion-controlling matrix (columns 7-8).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 38-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sachs et al [US 5,942,409]. Sachs et al discloses a cytosensor microphysiometer for screening and identifying biological effects or activity/inhibition of substances (see column 7, lines 45-59 and column 8). The substances are directed against urel-dependent mechanisms maintaining bacterial metabolism and viability in acidic media especially urel-dependent mechanisms of Helicobater pylori urease activation (see column 4, lines 12-65). Specifically, Sachs et al disclose a cytosensor layer consisting of a diffusion-controlling matrix such as agarose, with H. pylori cells

suspended therein. The cells are in aqueous diffusive contact with a light addressable potentiometric pH sensor, which assists in the detection process. The sensor is perfused with buffers (balanced salt solutions), HCl and supplemented with glucose and glutamine to regulate the vitality of the sensor cells, and thus influencing the detection sensitivity, selectivity of the matrix (see column 15, lines 16 to column 16). The primary sensor output is in voltage and changes in unit per time are calculated by a computer (see column 14, lines 43-63).

Sachs et al differ from the instant invention in failing to disclose the concentration, i.e. "about 2 to about 8 ml" or "about 3 to about 5 ml" as recited in claim 38 and 39, and optical density of cell suspensions, i.e. "about 0.6 to about 1.4" as recited in claims 40, and thickness of the sensor layer, i.e. "about 0.1 to about 10.0 mm", "about 0.5 to about 3mm", and "about 0.5 to about 0.8 mm", recited in claims 41-43.

However, the amount of layer composition, sensor layer concentration in proportion to the amount of cells present, and acceptable optical density of a plurality of cells in a composition are all result effective variables which Sachs et al has shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215,

218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claims 38-43 are for any particular purpose or solve any stated problem and the prior art teaches that sensors having membrane or film compositions may have different acceptable values dependent upon the method or purpose it is used, concentrations and parameters appear to work equally as well.

Absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by Sachs et al by normal optimization procedures known in the art.

10. Claims 38-40, 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Susuki et al (US 4,939,098). Susuki et al disclose a sensor device for the analysis of a sample fluid. The sensor device comprises a diffusion-controlling matrix composed of agarose or a synthetic polymer immobilizing reagents comprising antibodies, antigen, erythrocytes or liposomes, capable of producing multiple signals (immunoreaction, fluorescence, color changes, outflow from capsules) in response to the presence of a substance (a component of a blood sample) (column 2, lines 35-65, column 4, lines 50-68 and column 5) which can be measured optically via fluorescence or radiation and electrically (column 4, lines 50-52). The thickness of the diffusion-controlling matrix taught by Susuki is selected depending on purpose of use, but is typically 1-2 mm (column 3, lines 25-33). The sensor device is also comprised of a glass support (column 2, lines 66-68 and column 3, lines 31-33) and a carrier in contact with the diffusion-controlling matrix in which a sample is to be developed (column 5, lines 13-18). Phosphate

buffer are used as electrophoresis buffer, thus influencing the kinetics of the diffusion-controlling matrix (columns 7-8).

Susuki et al differ from the instant invention in failing to disclose the concentration, i.e. "about 2 to about 8 ml" or "about 3 to about 5 ml" as recited in claim 38 and 39, and optical density of cell suspensions, i.e. "about 0.6 to about 1.4" as recited in claims 40, and thickness of the sensor layer "about 0.5 to about 0.8 mm" as recited in claim 43.

However, the amount of layer composition, sensor layer concentration in proportion to the amount of cells present, and acceptable optical density of a plurality of cells in a composition are all result effective variables which Susuki et al has shown may be altered in order to achieve optimum results.It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claims 38-40, 43 are for any particular purpose or solve any stated problem and the prior art teaches that sensors having membrane or film compositions may have different acceptable values dependent upon the method or purpose it is used, concentrations and parameters appear to work equally as well.

Absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by Susuki et al by normal optimization procedures known in the art.

Response to Arguments

11. Applicant's arguments with respect to claims 1-26 have been considered but are moot in view of the new ground(s) of rejection.

12. With respect to Sachs et al, applicants argue that Sachs does not teach a machine that employs a "sheet of diffusion-controlling matrix." This argument is not persuasive because the "sheet of diffusion-controlling matrix" is characterized in that the matrix is a gel such as agarose, polyacrylates or a viscous solution. Sachs teaches a cytosensor layer characterized by cells immobilized with agarose, thus forming the diffusion-controlling matrix, and trapped between two microporous membranes. Applicants further argue the instrument as disclosed by Sachs is incapable of "detecting the spatial distribution of signal(s) produced when (the substance being tested for) is in contact with at least one spatially-discrete area of said sheet of diffusion-controlling matrix". This argument is not persuasive as the cells are retained in the sensor chambers, and thus would be located in spatially discrete areas, producing spatially discrete signals.

In regard to claims 9-11, now found in new claims 38-43, although applicants maintain that Sachs discloses a very different system than that presently claimed, the limitations of the

system that is claimed are broad enough to read upon the system that Sachs discloses, and thus could be construed to be optimizing the Sachs system, as discussed in the rejection above.

Conclusion

13. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is 703-305-4508. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on 703-305-3399. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

NY
July 28, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
7/28/03